General

Guideline Title

Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system).

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 12. 49 p. (Diagnostics guidance; no. 21).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The MiniMed Paradigm Veo system is recommended as an option for managing blood glucose levels in people with type 1 diabetes only if:

- They have episodes of disabling hypoglycaemia despite optimal management with continuous subcutaneous insulin infusion, and
- The company arranges to collect, analyse and publish data on the use of the of the MiniMed Paradigm Veo system (see Section 7.1 in the original guideline document)

The MiniMed Paradigm Veo system should be used under the supervision of a trained multidisciplinary team who are experienced in continuous subcutaneous insulin infusion and continuous glucose monitoring (CGM) for managing type 1 diabetes only if the person or their carer:

- Agrees to use the sensors for at least 70% of the time
- Understands how to use it and is physically able to use the system and
- Agrees to use the system while having a structured education programme on diet and lifestyle, and counselling

People who start to use the MiniMed Paradigm Veo system should only continue to use it if they have a decrease in the number of hypoglycaemic episodes that is sustained. Appropriate targets for such improvements should be set.

The Vibe and G4 PLATINUM CGM system shows promise but there is currently insufficient evidence to support its routine adoption in the National Health Service (NHS) for managing blood glucose levels in people with type 1 diabetes. Robust evidence is needed to show the clinical

effectiveness of using the technology in practice.

People with type 1 diabetes who are currently provided with the MiniMed Paradigm Veo system or the Vibe and G4 PLATINUM CGM system by the NHS for clinical indications that are not recommended in this National Institute of Health and Care Excellence (NICE) guidance should be able to continue using them until they and their NHS clinician consider it appropriate to stop.

Note: During the development of this guidance, NICE became aware that a new integrated sensor-augmented pump therapy system, the MiniMed 640G system (Medtronic), has become available. The evidence for the MiniMed 640G system has not been assessed in the guidance, and the recommendations, therefore, do not relate to its routine use in the NHS. For further information on the MiniMed 640G system please see the related NICE Medtech innovation briefing .

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Type 1 diabetes

Guideline Category

Management

Technology Assessment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system for managing blood glucose levels in people with type 1 diabetes

Target Population

People with type 1 diabetes

Interventions and Practices Considered

Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes

- MiniMed Paradigm Veo system
- Vibe and G4 PLATINUM CGM system

Major Outcomes Considered

- Main outcomes
  - Glycated haemoglobin (HbA1c, change from baseline, and number of participants achieving specified level of control)
  - Frequency of hyperglycaemia events and number of hyperglycaemia episodes, stratified by severity into mild and severe where data are available
  - Frequency of (nocturnal) hypoglycaemia events and number of hypoglycaemia episodes, stratified by severity into mild and severe where data are available
- Possible secondary outcomes
  - Mean blood glucose levels including fasting glucose levels
  - Postprandial glucose level
  - Amount of insulin being administered
  - Episodes of diabetic ketoacidosis and number of ketone tests
  - Health-related quality of life
  - Long-term complications of diabetes and treatment including retinopathy, neuropathy, cognitive impairment and end stage renal disease
  - Morbidity and mortality
  - Adverse events from testing, false results, treatment and sequelae
  - Acceptability of testing and method of insulin administration
  - Anxiety about experiencing hypoglycaemia
  - Costs, including support from health professionals
- In pregnant women, additional type 1 diabetes-related clinical outcomes
  - Premature birth
  - Macrosomia (excessive birth weight)
  - Respiratory distress syndrome in newborn
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review of the technology considered in this diagnostic guidance and prepare a

diagnostics assessment report (DAR). The DAR for this diagnostic appraisal was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Systematic Review Methods

A systematic review was conducted to summarise the evidence on the clinical effectiveness of the MiniMed Paradigm Veo System and the Vibe and G4 PLATINUM CGM system for the management of type 1 diabetes in adults and children. Systematic review methods followed the principles outlined in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care, and NICE Diagnostic Assessment Programme manual (see the "Availability of Companion Documents" field).

Inclusion and Exclusion Criteria

Participants

Study populations eligible for inclusion were adults, including pregnant women, and children with type 1 diabetes.

Setting

The relevant setting is self-use supervised by primary or secondary care.

Interventions

The main intervention technology for this appraisal was:

- MiniMed Paradigm Veo with continuous glucose monitoring (CGM) System and suspend function

In addition the Assessment Group included fully integrated insulin pump systems as an alternative technology, including the only existing fully integrated system currently available in the UK:

- The Vibe and G4 PLATINUM CGM system

Comparators

The scope as defined by NICE, specified the following comparator technologies:

- Capillary blood testing with continuous subcutaneous insulin infusion
- Capillary blood testing with multiple daily insulin injections
- CGM with continuous subcutaneous insulin infusion (non-integrated)
- CGM with multiple daily injections

Studies comparing continuous subcutaneous insulin infusion (CSII) with multiple daily insulin injections (MDI) often use different types of monitoring (self-monitoring of blood glucose [SMBG] or CGM). Unless results were reported separately for the different types of monitoring, these studies were excluded from the review, because they do not allow a comparison of a relevant intervention with the comparators. The same applies to studies comparing CGM with SMBG, without specifying the type of insulin device (CSII or MDI) used.

Outcomes

Refer to the "Major Outcomes Considered" field.

Study Design

- Randomised controlled trials (RCTs) or controlled clinical trials (CCTs) where no RCTs are available for comparisons of interventions and comparators
- Observational studies for additional information for interventions, if no RCTs are found

Subgroup Analyses

If evidence and the structure of the cost-effectiveness model permit, the following subgroups may be explored:

- Pregnant women, and women planning pregnancy (not including gestational diabetes)
- People who need to self-monitor their blood glucose level more than 10 times a day

- People with type 1 diabetes who are having difficulty managing their condition. These difficulties include:
  - Not maintaining the recommended HbA1c level of 8.5% (69.4 millimoles/mole) or below
  - Nocturnal hypoglycaemia
  - Impaired awareness of hypoglycaemia
  - Severe hypoglycaemia defined as having low blood glucose levels that requires assistance from another person to treat

Search Strategy

Systematic literature searches were conducted to identify studies about sensor-augmented pump therapy for type 1 diabetes (specifically the MiniMed Paradigm Veo system, and the Vibe and G4 Platinum system), as well as RCTs and economic evaluations of insulin pump/infusion therapy and multiple daily injections for type 1 diabetes. Search strategies were developed using the recommendations of the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care, and the Cochrane Handbook. The search strategies combined relevant search terms comprising indexed keywords (e.g., Medical Subject Headings [MeSH] and EMTREE) and free text terms appearing in the titles and/or abstracts of database records. Search terms were identified through discussion between the review team, by scanning background literature and 'key articles' already known to the review team, and by browsing database thesauri. The search strategies were structured using search terms for 'type 1 diabetes' in combination with search terms for 'sensor-augmented pump therapy'. Two further facets of search terms were included to capture 'insulin infusion' and 'multiple daily injections'. In addition, the search strategy for clinical effectiveness studies included a sensitive methodological search filter designed to identify RCTs. The EMBASE search strategy was translated to run effectively in each of the databases searched. No date or language limits were applied. The main EMBASE search strategies were independently peer reviewed by a second Information Specialist using the Canadian Agency for Drugs and Technologies (CADTH) Peer Review checklist.

The full search strategies are presented in Appendix 1 of the DAR.

The following databases and resources were searched for relevant RCTs, systematic reviews and health technology assessments:

- MEDLINE (OvidSP): 1946-2014/Aug week 4
- MEDLINE In-Process Citations and Daily Update (OvidSP): up to 2014/09/04
- PubMed (NLM): up to 2014/09/05
- EMBASE (OvidSP): 1974-2014/week 34
- Cochrane Database of Systematic Reviews (CDSR) (Wiley Online Library): issue 9/Sep 2014
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley Online Library): issue 8/Aug 2014
- Database of Abstracts of Reviews of Effects (DARE) (Wiley Online Library): issue 3/Jul 2014
- Health Technology Assessment Database (HTA) (Wiley Online Library): issue 3/Jul 2014
- Science Citation Index (SCI) (Web of Science): 1988-2014/08/29
- LILACS (Latin American and Caribbean Health Sciences Literature) (http://lilacs.bvsalud.org/en/): 1982-2014/09/05
- National Institute for Health Research (NIHR) Health Technology Assessment Programme (www.hta.ac.uk/): up to 2014/09/05
- PROSPERO (http://www.crd.york.ac.uk/prospero/): up to 2014/09/05
- U.S. Food and Drug Administration (FDA) (www.fda.gov): up to 2014/09/05
- Medicines and Healthcare Products Regulatory Agency (MHRA) (https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency): up to 2014/09/05

Completed and ongoing trials were identified by searches of the following trials registries:

- National Institutes of Health (NIH) ClinicalTrials.gov (http://www.clinicaltrials.gov/): up to 2014/09/02
- Current Controlled Trials (http://www.controlled-trials.com/) (now the ISRCTN registry): up to 2014/09/05
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/): up to 2014/09/05

The following conference proceedings were searched: Diabetes UK, European Association for the Study of Diabetes (EASD) and American Diabetes Association (ADA).

The bibliographies of identified research and review articles were checked for relevant studies. As a number of databases were searched, there was some degree of duplication. In order to manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote reference management software and duplicate records removed. Rigorous records were maintained as part of the searching process. Individual records within the EndNote reference libraries were tagged with searching information, such as searcher, date searched, database host,

database searched, search strategy name and iteration, theme and search question. This enabled the information specialist to track the origin of each individual database record, and its progress through the screening and review process.

Inclusion Screening

Two reviewers independently screened the titles and abstracts of all reports identified by searches and any discrepancies were discussed and resolved by consensus. Full text copies of all studies deemed potentially relevant, after discussion, were obtained and the same two reviewers independently assessed these for inclusion; any disagreements were resolved by consensus. Details of studies excluded at the full paper screening stage are presented in Appendix 4 of the DAR.

Results of Literature Searches

The literature searches of bibliographic databases identified 9,870 references. After initial screening of titles and abstracts, 555 were considered to be potentially relevant and ordered for full paper screening. Of the total of 555 publications considered potentially relevant, 29 could not be obtained within the time scale of this assessment. Most of these 29 unobtainable studies were older (pre-2000) or conference abstracts; only four were possibly relevant trials published after 2000 and based on their abstracts it was unclear whether they fulfilled the inclusion criteria. Figure 1 of the DAR shows the flow of studies through the review process, and Appendix 4 of the DAR provides details, with reasons for exclusions, of all publications excluded at the full paper screening stage.

Assessment of Cost-effectiveness

Review of Economic Evaluations

Search Methods

Literature searches were undertaken to identify published economic evaluations for MiniMed Veo and Animas Vibe. The search strategy for economic evaluations included a filter designed to identify cost and economic studies in those databases that are not health economic specific.

The following databases and resources were searched for relevant economic evaluations and cost studies:

- National Health Service Economic Evaluation Database (NHS EED) (Wiley Online Library): issue 3/Jul 2014
- Health Economic Evaluations Database (HEED) (Wiley Online Library): up to 2014/09/05
- MEDLINE (OvidSP): 1946-2014/Aug week 4
- MEDLINE In-Process Citations and Daily Update (OvidSP): up to 2014/09/05
- PubMed (NLM): up to 2014/09/05
- EMBASE (OvidSP): 1974-2014/week 34
- EconLit (EBSCO): 1969-20140801
- CEA Registry (www.cearegistry.org): up to 2014/09/05
- Research Papers in Economics (RePEc) (http://repec.org/): up to 2014/09/05

In addition economic searches specifically for MiniMed Paradigm Veo and Animas Vibe were conducted using the same resources listed above.

The full search strategies are presented in Appendix 1 of the DAR.

Relevant studies were then identified in two stages. Titles and abstracts returned by the search strategy were examined independently by two researchers and screened for possible inclusion. Disagreements were resolved by discussion. Full texts of the identified studies were obtained. The same two researchers examined these independently for inclusion or exclusion, and disagreements were resolved by discussion.

Inclusion Criteria

The initial search identified a total of eight abstracts, six of which were of conference abstracts and thus not included. Both of the full papers were identified as relevant to the review. One study evaluated Animas Vibe (integrated CSII+CGM) versus multiple daily insulin injection (MDI) + self-monitoring of blood glucose (SMBG) in the US, whereas the other study evaluated the MiniMed Paradigm Veo (CSII+CGM+Suspend) versus CSII+SMBG in Australia. The first evaluation showed that the Animas Vibe was not cost-effective compared to multiple daily injections despite taking all health effects into account through the IMS CORE (Center for Outcomes Research) diabetes model (IMS CDM). On the other hand, the second study showed that the MiniMed Veo system was cost-effective compared to continuous subcutaneous insulin infusion, whilst only taking the impact of the reduction of severe hypoglycaemic events into account. The characteristics of these studies are summarised in Table 24 of the DAR.

Of the six (excluded) conference abstracts one was an abstract that was later published as full paper and already included in one of the two

selected full papers.

Number of Source Documents

Clinical Effectiveness

Fifty-four publications of 19 studies were included in the review. In addition, 19 publications of 18 ongoing studies were found. These are described in Chapter 4.2.6 of the Diagnostics Assessment Report (see the "Availability of Companion Documents" field).

Cost-effectiveness

- Two existing studies were included.
- An economic model was submitted by the External Assessment Group.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review of the technology considered in this diagnostic guidance and prepare a diagnostics assessment report (DAR). The DAR for this diagnostic guidance was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Systematic Review Methods

Data Extraction

Data relating to study details, participants, intervention and comparator tests, and outcome measures were extracted by one reviewer, using a piloted, standard data extraction form. A second reviewer checked data extraction and any disagreements were resolved by consensus.

Quality Assessment

The methodological quality of included studies was assessed using standard tools. The assessment of the methodological quality of each included study was based on the Cochrane Collaboration quality assessment checklist as detailed in Table 1 of the DAR. Each study was awarded a 'yes', 'no' or 'unclear/unknown' rating for each individual item in the checklist. Any additional clarifications or comments were also recorded.

Quality assessment was carried out independently by two reviewers. Any disagreements were resolved by consensus. The results of the quality assessment were used for descriptive purposes to provide an evaluation of the overall quality of the included studies and to provide a transparent method of recommendation for design of any future studies. Based on the findings of the quality assessment, recommendations are made for the conduct of future studies.

Methods of Analysis/Synthesis

Where meta-analysis was considered unsuitable for some or all of the data identified (e.g., due to the heterogeneity and/or small numbers of studies), the Assessment Group employed a narrative synthesis. Typically, this involves the use of text and tables to summarise data. These allow the reader to consider any outcomes in the light of differences in study designs and potential sources of bias for each of the studies being reviewed. Studies were organised by comparison.

The methods used to synthesise the data were dependent on the types of outcome data included and the clinical and statistical similarity of the studies. Possible methods include the following types of analysis.

Dichotomous Outcomes

Dichotomous data were analysed by calculating the relative risk (RR) for each trial using the DerSimonian and Laird random effects method and the corresponding 95% confidence intervals (CIs).

Continuous Outcomes

Continuous data were analysed by calculating the weighted mean difference (WMD) between groups and the corresponding 95% CI. If the standard deviations and means were not determinable, they were estimated from the data that was provided or using a representative value from other studies.

Systematic differences between studies (heterogeneity) are likely; therefore, the random-effects model was used for the calculation of RRs or WMDs. Heterogeneity was initially assessed by measuring the degree of inconsistency in the studies' results (I^2).

If important heterogeneity was identified, the Assessment Group planned to formally investigate this using meta-regression. In particular, a model was planned to be used to explore the possible modifying effects of the following pre-specified factors: methodological quality of the primary studies, underlying illness, and different age groups. The coefficient describing the predictive value of each factor and the overall effect on the main outcome would be modelled, using a fixed-effect model. However, due to the limited number of studies for each comparison this was not possible.

A funnel plot (plots of logarithm of the RR for efficacy against the precision of the logarithm of the RR) was planned in order to estimate potential asymmetry, which would be indicative of small study effects. Glycated haemoglobin (HbA1c) was chosen as an outcome since this is likely to be reported by the majority of included studies. In addition, the Egger regression asymmetry test was planned in order to facilitate the prediction of potential publication biases. This test detects funnel plot asymmetry by determining whether the intercept deviates significantly from zero in a regression of the standardised effect estimates against their precision. However, due to the limited number of studies for each comparison this was not possible.

Network Meta-analysis Methods

In the absence of randomised controlled trials (RCTs) directly comparing the MiniMed Veo System or the integrated continuous subcutaneous insulin infusion (CSII) + continuous glucose monitoring (CGM) system with the comparators, indirect treatment comparisons were performed, where possible. As only limited networks could be formed a mixed treatment comparison was not possible. However, where it was possible indirect comparisons were made. Dependent on the data available, separate network analyses were performed for each of the subgroups specified in this protocol. Indirect meta-analysis were performed using Microsoft Excel 2007 according to the method developed by Bucher 1997. Effect sizes with 95% CIs were calculated using results from the direct head-to-head meta-analysis. Direct head-to-head meta-analyses were performed using random effects models in STATA (STATA™ for Windows, version 13, Stata Corp; College Station, TX).

See Section 4 of the DAR for additional information on clinical effectiveness analysis.

Assessment of Cost-effectiveness

Quality Assessment

A quality appraisal was carried out on the two studies, using the Drummond checklist. A summary of the results is provided in Table 26 in the DAR.

Model Structure and Methodology

The IMS CORE (Center for Outcomes Research) diabetes model (IMS CDM) was chosen to perform the cost-effectiveness analyses in this assessment. Because this model is not appropriate for the health economic outcomes for paediatric/adolescent populations and pregnant women, these two subgroup populations were not included in the cost-effectiveness analyses.

Model Structure

The IMS CDM is an internet based, interactive simulation model that predicts the long-term health outcomes and costs associated with the management of type 1 diabetes mellitus (T1DM) and type 2 DM (T2DM).

The structure of the IMS CDM is shown in Figure 10 of the Assessment Report. The IMS CDM comprises 17 interdependent sub-models, which represent the most common diabetes-related complications: angina pectoris, myocardial infarction (MI), congestive heart failure (CHF), stroke, peripheral vascular disease (PVD), diabetic retinopathy, cataracts, hypoglycaemia, ketoacidosis, nephropathy, neuropathy, foot ulcer/amputation, macular oedema, lactic acidosis (T2DM only), (peripheral) oedema (T2DM only), and depression. A sub-model for non-specific mortality is also included. Each of these sub-models is a Markov model that includes different health states depicting the severity/stage of the complication. Transition probabilities in between the states of a complication sub-model can be time-, demographics-, state-, physiological factor- and diabetes type-dependent.

Additionally, the non-parametric bootstrapping approach provides additional information on the uncertainty surrounding the long-term outcomes provided by the model. In this approach, a cohort population (with a size that can be defined by the model user) is created. Each patient in this population is unique in the sense of its baseline characteristics (demographics, existing baseline complications, baseline physiological risk factors and other risk factors like the number of cigarettes smoked per day). Within the bootstrapping simulation approach, two types of analysis are possible: deterministic and probabilistic. In the deterministic simulation the continuous input parameters (baseline age, diabetes duration, HbA1c, etc.) of each patient in the cohort that is created (say 1,000 patients) will be identical, but binary variables will differ (gender, presence of a diabetes-related complication like MI, etc.). In each iteration, one of the patients in this cohort is sampled with replacement and entered into the simulation (i.e., the complication sub-models) until the patient dies. Applied treatment effects, utilities, costs, coefficients of cardiovascular disease (CVD) events will be then identical in each iteration. However, results will differ per iteration due to the differences in the binary input parameters in the baseline cohort and the way a patient progresses through the model (random walk). In the probabilistic simulation all variables that are subjected to random sampling (i.e., cohort baseline parameters, treatment effects, coefficients of the cardiovascular disease risk equations, health state utilities/adverse event disutilities, and costs) are randomly assigned at the beginning of the first iteration according to pre-defined probability distributions. Then all the patients in the cohort (say 1,000) are processed through the model while the parameters assigned at the start of the iteration are held constant. Those patients will only differ due to binary variables and random walk. When the model progresses to the next iteration, parameters are re-sampled again and the next 1,000 patients are progressed though the model while parameters are held constant again. This process is repeated for all the bootstrap iterations.

See Section 5 of the DAR for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Developing Recommendations

After reviewing the evidence the Diagnostic Advisory Committee (DAC) agrees draft recommendations on the use of the technology in the National Health Service (NHS) in England. When formulating these recommendations, the Committee has discretion to consider those factors it believes are most appropriate to the evaluation. In doing so, the Committee has regard to any relevant provisions of the National Institute for Health and Care Excellence's (NICE's) Directions, set out by the Secretary of State for Health, and legislation on human rights, discrimination and equality. In undertaking evaluations of healthcare technologies, NICE takes into account the broad balance of clinical benefits and costs, the degree of clinical need of patients under consideration, any guidance issued to the NHS by the Secretary of State that is specifically drawn to the attention of NICE by the Secretary of State, and any guidance issued by the Secretary of State, and the potential for long-term benefits to the NHS of innovation.

The Committee takes into account advice from NICE on the approach it should take to making scientific and social value judgements. Advice on social value judgements is informed in part by the work of NICE's Citizens Council.

The Committee takes into account how its judgements have a bearing on distributive justice or legal requirements in relation to human rights, discrimination and equality. Such characteristics include, but are not confined to: race, gender, disability, religion or belief, sexual orientation, gender reassignment and pregnancy or maternity.

The Committee considers the application of other Board-approved NICE methods policies, such as the supplementary guidance on discounting and the end-of-life criteria, if they are relevant to the evaluation.

Because the Programme often evaluates new technologies that have a thin evidence base, in formulating its recommendations the Committee balances the quality and quantity of evidence with the expected value of the technology to the NHS and the public.

The credibility of the guidance produced by NICE depends on the transparency of the DAC's decision-making process. It is crucial that the DAC's decisions are explained clearly, and that the contributions of registered stakeholders and the views of members of the public are considered. The reasoning behind the Committee's recommendations is explained, with reference to the factors that have been taken into account.

The language and style used in the documents produced by the Committee are governed by the following principles:

- Clarity is essential in explaining how the DAC has come to its conclusions.
- The text of the documents does not need to reiterate all the factual information that can be found in the information published alongside the guidance. This needs careful judgement so that enough information and justification is given in the recommendations to enable the reader to understand what evidence the DAC considered and, if appropriate, who provided that evidence.

The Committee may take into account factors that may provide benefits to the NHS or the population, such as patient convenience. It may also consider costs and other positive or negative impacts on the NHS that may not be captured in the reference-case cost analysis, such as improved processes.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The Diagnostics Advisory Committee considered the cost-effectiveness analyses for the MiniMed Paradigm Veo system. It noted that 3 base cases were available, but that none included a comparison with continuous glucose monitoring (CGM) and multiple daily injections because of a lack of clinical-effectiveness data. The Committee noted that the cost-effectiveness analyses were done using the IMS CORE Diabetes Model. It discussed the advantages and disadvantages of the model, and heard from experts that although the model was well validated its structure and underlying clinical data were likely to favour interventions that are aimed at reducing glycated haemoglobin (HbA1c) and associated long-term complications. The Committee heard from the External Assessment Group that the impacts of short-term outcomes associated with hypoglycaemic events are more difficult to capture in the model because, unlike change in HbA1c, the rate of hypoglycaemia cannot be changed over time. The Committee also heard from clinical specialists that the risk equations included in the model were dated and may underestimate the risk of long-term complications for people with type 1 diabetes. The Committee concluded that despite its extensive validation, the IMS CORE Diabetes Model may not be suitable for investigating the impact of interventions on short-term clinical outcomes, and that it was likely that this impact could have been undervalued in the analyses.

The Committee considered the treatment-effect estimates that had been used in the economic modelling. It noted that these treatment effects were limited by the heterogeneity in the meta-analyses constructed for the economic model. It heard from clinical specialists that in the mixed population base case, it was implausible that HbA1c increases from baseline with continuous subcutaneous insulin infusion because this is an intervention that is intended to reduce HbA1c. Further, it also heard that for the population who experience hypoglycaemia, the assumption that the hypoglycaemic event rate is equivalent for capillary blood testing with continuous subcutaneous insulin infusion and CGM with continuous subcutaneous insulin infusion was likely to be implausible because the addition of CGM is intended to reduce the occurrence of hypoglycaemia. The Committee concluded that, in general, the cost-effectiveness analyses could not be considered robust because the insufficient evidence base for clinical effectiveness leads to a large amount of uncertainty in the incremental clinical-effect estimates.

See Sections 5 and 6 in the original guideline document for additional discussion of cost effectiveness.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

The National Institute for Health and Care Excellence (NICE) sends the Diagnostics Assessment Report (DAR), with any confidential material removed, to registered stakeholders for comment. Stakeholders have 10 working days to return comments. Models supporting the DAR are made available to registered stakeholders on request during this period.

NICE presents anonymised registered stakeholder comments on the DAR, along with any responses from NICE or the External Assessment Group, to the Committee and later publishes these comments on its Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Diagnostics Advisory Committee (DAC) considered a systematic review and an economic model prepared by an External Assessment Group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Using these integrated sensor-augmented pump therapy systems may improve glucose control and consequently may reduce the number of diabetes-related complications and improve the quality of life for people with type 1 diabetes. They may also make it easier for people to adhere to treatment. The ability of the MiniMed Paradigm Veo system to automatically suspend insulin delivery may help to reduce the incidence of severe and nocturnal hypoglycaemia, and its associated anxiety. Both systems may also offer benefits to the National Health Service (NHS) through cost and resource savings by reducing the number of hospital admissions and consultations for diabetes-related complications, and by achieving optimum blood glucose control more quickly.

Potential Harms

The studies reviewed for this guideline showed no device-related serious adverse events.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools, in association with relevant stakeholders, to help organisations put this guidance into practice. In addition NICE will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be considered by the NICE Medical Technologies Evaluation Programme research facilitation team for the development of specific research study protocols as appropriate. NICE will also incorporate the research recommendations (see Section 7 of the original guideline document) into its guidance research recommendations database (available on the NICE Web site) and highlight these recommendations to public research bodies.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 12. 49 p. (Diagnostics guidance; no. 21).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb 12

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Diagnostics Advisory Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Committee members are required to submit a declaration of interests on appointment, in every year of their tenure, and at each Committee meeting, in line with the National Institute for Health and Care Excellence's (NICE's) code of practice for declaring and dealing with conflicts of interest.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub or eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 12 p. (Diagnostics guidance; no. 21). Available from the NICE Web site .
- Diagnostics Assessment Programme. Evidence overview. Type 1 diabetes: integrated sensor-augmented pump therapy systems for managing blood glucose levels (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). Diagnostics assessment report. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Mar. 571 p. Available from the NICE Web site .
- NICE diagnostics adoption support for type 1 diabetes: Integrated sensor-augmented pump therapy systems for managing blood glucose levels (The MiniMed Paradigm Veo System and the Vibe and G4 PLATINUM CGM system) – insights from the NHS. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 22 p. Available from the NICE Web site .
- Diagnostics Assessment Programme manual. London (UK): National Institute for Health and Care Excellence; 2011 Dec. 130 p. Available from the NICE Web site .

Patient Resources

The following is available:

- Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system). Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available in Welsh from the NICE Web site .

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